

Transmittal Letter to the United States
Designated/Elected Office (DO/EO/US)

10/070672 1
FORM PTO-1390

Docket No. : **FI-38PCT**
U.S. Application No. :
International Application No. : **PCT/EP00/08645**
International Filing Date. : **September 5, 2000**
Priority Dates Claimed : **September 6, 1999**
Title of Invention : **METHOD FOR IMPROVING AND MAINTAINING BOWEL FUNCTION
AS WELL AS A METHOD FOR THE PRODUCTION THEREOF**
Applicant(s) for (DO/EO/US) : **Günther Beisel**

JCO7 Rec'd PCT/PTO 06 MAR 2002

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

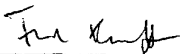
1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures 35 U.S.C. 371 (f) at any time rather than delay examination until the expiration of the applicable time limit set forth in 35 U.S.C 371(b) and PCT Articles 22 and 39(1).
4. ☐ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed [35 U.S.C. 371(c)(2)].
 - a) ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
 - b) ☐ has been transmitted by the international Bureau.
 - c) ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ A translation of the International Application into English [35 U.S.C.371(c)(2)].
7. ☐ Amendments to the claims of the International Application under PCT Article 19 [35 U.S.C.371(c)(3)].
 - a) ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b) ☐ have been transmitted by the International Bureau.
 - c) ☐ have not been made; however, the time limit for making such amendments has **NOT** expired.
 - d) ☐ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 [35 U.S.C.371(c)(3)].
9. ☒ An oath or declaration of the inventor(s) [35 U.S.C.371(c)(4)]. **UNSIGNED**
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 [35 U.S.C.371(c)(5)].

Items 11. to 16. below concern other document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 C.F.R. 1.97 and 198.
12. ☐ An Assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A **FIRST** preliminary amendment.
☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ (other items or information) **PTO-1449 w/ 8 references and International Search Report**

EXPRESS MAIL No.: EU 076 175 262 US Deposited: March 6, 2002

I hereby certify that this correspondence is being deposited with the United States Postal Service Express mail under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, DC 20231.


Friedrich Kueffner

March 6, 2002
Date

U.S. Application No. (if known, see 37 C.F.R. 1.50):
International Application No. : PCT/EP00/08645

10/070672

Page 2
Docket No: FI-38PCT

17. ☒ The following fees are submitted:

BASIC NATIONAL FEE [37 CFR 1.492(a)(1)-(5)]:

- ☒ Search Report has been prepared by the EPO or JPO..... \$ 890.00
- ☐ International preliminary examination fee paid to USPTO [37 CFR 1.482]:..... \$ 710.00
- ☐ No International preliminary examination fee paid to USPTO [37 CFR 1.482]
but International search fee paid to USPTO [37CFR 1.445(a)(2)]:..... \$ 740.00
- ☐ Neither International preliminary examination fee [37 CFR 1.482] nor
International search fee [37 CFR 1.445(a)(2)] paid to USPTO:..... \$ 1040.00
- ☐ International preliminary examination fee paid to USPTO [37 CFR 1.482]
and all claims satisfied provisions of PCT Article 33 (2) to (4):..... \$ 100.00

ENTER APPROPRIATE BASIC FEE AMOUNT: \$ 890.00

Surcharge of \$ 130.00 for furnishing the oath or declaration later than 20 30 months
from the earliest claimed priority date [37 CFR 1.492(e)]

Claims	filed	Extra	Rate
Total Claims	20	-20=	x \$ 18 =
Indep. Claims	1	- 3=	x \$ 84 =
Multiple Dependent Claims (if applicable) + \$ 280 =			

TOTAL OF ABOVE CALCULATIONS: \$ 890.00

Small Entity Status is claimed.

(divided by 2)

445.00

SUBTOTAL: \$ 445.00

Processing fee of \$ 130.00 for furnishing the English translation later than 20 30 months
from the earliest claimed priority date [37 CFR 1.492(f)]

TOTAL NATIONAL FEE: \$ 445.00

Fee for recording the enclosed assignment [37 CFR 1.21(h)] the assignment must be
accompanied by an appropriate cover sheet [37 CFR 3.28,3.31]. \$ 40.00 per property

TOTAL FEES ENCLOSED: \$ 445.00

AMOUNT TO BE REFUNDED: Refunded \$

AMOUNT TO BE CHARGED: Charged \$

a) ☒ A check in the amount of \$ 445.00 to cover the above fees is enclosed.

b) ☐ Please charge my Deposit Account No. 11-1835 in the amount of \$ to cover the above fees.
A duplicate copy of this sheet is enclosed.

c) ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any
overpayment to Deposit Account No. 11-1835. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 36 CFR 1.494 or 1.495 has not been met, a petition to revive [37 CFR 1.137(a) or (b)] must
be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Friedrich Kueffner
317 Madison Avenue
Suite 910
New York, NY 10017

Friedrich Kueffner
Name


signature

29,482
Reg. No.

March 6, 2002
Date

JC19 Rec'd PCT/PTO 06 MAR 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

FI-38PCT

Applicant(s) : Günther Beisel
Serial No. : NOT YET KNOWN (PCT/EP00/08645)
Int. Filed : September 5, 2000
For : METHOD FOR IMPROVING AND MAINTAINING BOWEL
FUNCTION AS WELL AS A METHOD FOR THE
PRODUCTION THEREOF

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

S I R:

In advance of the first office action, please amend the claims
as follows:

IN THE CLAIMS

Replace current claims 1 - 20 by the enclosed amended claims
1 - 20. A marked-up version of amended claims 1 - 20 is also enclosed.

REMARKS

Claims 1 - 20 are in the application.

As a result of the foregoing amendment, the claims have been
amended to remove improper multiple dependencies.

Any additional fees or charges required at this time in connection
with the application may be charged to our Patent and Trademark Office
Deposit Account No. 11-1835.

Respectfully submitted,

F. Kueffner

Friedrich Kueffner Reg. No. 29,482
317 Madison Avenue
New York, NY 10017
(212) 986-3114

March 6, 2002

FK:ml

ENCLS:

**Amended Claims;
Marked-Up Version.**

EXPRESS MAIL No.: **EU 076 175 262 US**

Deposited: **March 6, 2002**

I hereby certify that this correspondence is being deposited with the United States Postal Service Express mail under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, DC 20231.

F. Kueffner

Friedrich Kueffner

CLEAN VERSION OF AMENDED CLAIMS

1. A composition for improving and maintaining intestinal activity and/or for improving and/or normalizing bowel movements, wherein it comprises a material which, if it is degradable in the stomach and/or small intestine, is provided with a compound which does not dissolve until in the intestine, and is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine.
2. The composition as claimed in claim 1, wherein the material has three-dimensional polymeric networks.
3. The composition as claimed in claim 1, wherein the material is in the form of a sponge-like structure.
4. The composition as claimed in claim 1, wherein the material is coated with the compound.
5. The composition as claimed in claim 1, wherein the material is introduced into a container which consists of a compound which is exclusively soluble in intestine.

6. The composition as claimed in claim 1, wherein the compound introduced is introduced into the material.
7. The composition as claimed in claim 1, wherein the compound is soluble in liquid having a pH from 5 to 10.
8. The composition as claimed in claim 1, wherein the compound is soluble in liquids having a pH from 5.5 to 8.5.
9. The composition as claimed in claim 1, wherein the compound is soluble in liquids having a pH from 6.4 ± 0.6 to 7.0 ± 0.7 .
10. The composition as claimed in claim 1, wherein the material comprises natural, semisynthetic or synthetic polymers and also stably crosslinked bodies or combinations thereof.
11. The composition as claimed in claim 1, wherein the material comprises collagen, cellulose or alginate.
12. The composition as claimed in claim 1, wherein the material is compressible to one half to one hundredth, preferably one quarter to one fiftieth, particularly preferably one tenth to one twentieth of its original size.

13. The composition as claimed in claim 1, wherein the material can be decompressed in the intestine to two to one hundred times, preferably four to fifty times, particularly preferably ten to twenty times, its size in the compressed state.
14. The composition as claimed in claim 1, wherein it comprises pharmaceutically and/or biologically active substances, laxatives, nutrients or food supplements, foodstuffs, taste or stimulant substances, flavorings or other ancillary substances.
15. The composition as claimed in claim 1 for use for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements, wherein it comprises a material which, if it is degradable in the stomach and/or small intestine, is provided with a compound which does not dissolve until in the intestine and is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine.

16. A process for preparing a composition for improving and maintaining intestinal activity as claimed in claim 1, wherein
- a) a suspension of the material is prepared,
 - b) from this suspension a sponge-like or foam-like structure is prepared by methods known per se,
 - c) the material is then reversibly compressed,
 - d) before, during or after step b) the material is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine and
 - e) if appropriate a compound is applied to this material and/or a compound is introduced into the material and/or this material is encased with such a compound, with this compound not dissolving until in the intestine.
17. The use of the composition as claimed in claim 1 for preparing compositions for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements.
18. The use of the composition as claimed in claim 1 for preparing pharmaceutically active compositions and/or nutrients and/or food supplements and/or (dietetic) foods.

19. The use of the composition as claimed in claim 1 for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements and/or for reducing the transit time of the chyme in the intestine, combined with a prophylactic or laxative action.
20. The use of the composition as claimed in claim 1 in the fields of pharmacy and/or health and/or for nutrition and/or food supplementation.

MARKED-UP VERSION OF AMENDED CLAIMS

1. A composition for improving and maintaining intestinal activity and/or for improving and/or normalizing bowel movements, [characterized in that] wherein it comprises a material which, if it is degradable in the stomach and/or small intestine, is provided with a compound which does not dissolve until in the intestine, and is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine.
2. The composition as claimed in claim 1, [characterized in that] wherein the material has three-dimensional polymeric networks.
3. The composition as claimed in [either of claims 1 or 2, characterized in that] claim 1, wherein the material is in the form of a sponge-like structure.
4. The composition as claimed in [one of claims 1 to 3, characterized in that] claim 1, wherein the material is coated with the compound.
5. The composition as claimed in [one of claims 1 to 4, characterized in that] claim 1, wherein the material is introduced into a container which consists of a compound which is exclusively soluble in intestine.

6. The composition as claimed in [one of claims 1 to 5, characterized in that] claim 1, wherein the compound introduced is introduced into the material.
7. The composition as claimed in [one of claims 1 to 6, characterized in that] claim 1, wherein the compound is soluble in liquid having a pH from 5 to 10.
8. The composition as claimed in [one of claims 1 to 7, characterized in that] claim 1, wherein the compound is soluble in liquids having a pH from 5.5 to 8.5.
9. The composition as claimed in [one of claims 1 to 8, characterized in that] claim 1, wherein the compound is soluble in liquids having a pH from 6.4 ± 0.6 to 7.0 ± 0.7 .
10. The composition as claimed in [one of claims 1 to 9, characterized in that] claim 1, wherein the material comprises natural, semisynthetic or synthetic polymers and also stably crosslinked bodies or combinations thereof.
11. The composition as claimed in [one of claims 1 to 10, characterized in that] claim 1, wherein the material comprises collagen, cellulose or alginate.

12. The composition as claimed in [one of claims 1 to 11, characterized in that] claim 1, wherein the material is compressible to one half to one hundredth, preferably one quarter to one fiftieth, particularly preferably one tenth to one twentieth of its original size.
13. The composition as claimed in [one of the preceding claims 1 to 12, characterized in that] claim 1, wherein the material can be decompressed in the intestine to two to one hundred times, preferably four to fifty times, particularly preferably ten to twenty times, its size in the compressed state.
14. The composition as claimed in [one of the preceding claims 1 to 13, characterized in that] claim 1, wherein it comprises pharmaceutically and/or biologically active substances, laxatives, nutrients or food supplements, foodstuffs, taste or stimulant substances, flavorings or other ancillary substances.
15. The composition as claimed in [one of claims 1 to 14] claim 1 for use for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements, [characterized in that] wherein it comprises a material which, if it is degradable in the stomach and/or small intestine, is provided with a compound

which does not dissolve until in the intestine and is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine.

16. A process for preparing a composition for improving and maintaining intestinal activity as claimed in [one of claims 1 to 15, characterized in that] claim 1, wherein
- a) a suspension of the material is prepared,
 - b) from this suspension a sponge-like or foam-like structure is prepared by methods known per se,
 - c) the material is then reversibly compressed,
 - d) before, during or after step b) the material is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine and
 - e) if appropriate a compound is applied to this material and/or a compound is introduced into the material and/or this material is encased with such a compound, with this compound not dissolving until in the intestine.

17. The use of the composition as claimed in [one of the preceding claims] claim 1 for preparing compositions for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements.
18. The use of the composition as claimed in [one of the preceding claims] claim 1 for preparing pharmaceutically active compositions and/or nutrients and/or food supplements and/or (dietetic) foods.
19. The use of the composition as claimed in [one of the preceding claims] claim 1 for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements and/or for reducing the transit time of the chyme in the intestine, combined with a prophylactic or laxative action.
20. The use of the composition as claimed in [one of the preceding claims] claim 1 in the fields of pharmacy and/or health and/or for nutrition and/or food supplementation.

WO 01/17509

- 1 -

PCT/EP00/08645

Composition for improving and maintaining intestinal
activity and process for its preparation

5 The present invention relates to a composition for improving and maintaining intestinal activity.

10 US 3,688,763 describes a method of collecting cellular material from the large intestine of humans. The patient swallows a capsule the outer coating of which together with the container situated beneath dissolves in the intestine and releases a compressed sponge which is then expelled via natural evacuation of the bowels. On its transport through the intestine, the sponge scrapes off outer cells of the intestinal lumen which are carried along to the outside. By this means, in a simple manner, intestinal cells are removed from the patient with the purposes of then studying these for tumors or cancer cells.

20 This system had the object of collecting intestinal cells for analytical purposes. However, targeted stimulation of intestinal activity is not achieved in this manner.

25 DE 4 025 912 discloses a composition for oral intake which consists of a receptacle which, in the stomach, can be dissolved and releases the contents. This receptacle is filled with a material which on being released in the stomach increases in volume and as a result induces in the person a feeling of satiation.

30 The disadvantage of this system is that it is directed solely toward filling the stomach. A stimulation of intestinal activity is thus not associated with it, however.

It is an object of the present invention to provide a composition comprising a material which is deformable

- 2 -

and, if appropriate, is form-reducible and/or reversibly compressible and which passes through the esophagus and the stomach and in the intestine releases a stimulating action on the intestinal activity.

5

This object is achieved by means of the fact that the composition comprises a material which, if it is degradable in the stomach and/or small intestine it is provided with a compound which does not dissolve until
10 in the intestine and which is loaded with active compounds, for example for prophylaxis, or with laxatives, in such a manner that these are predominantly or exclusively not released until in the intestine.

15

Preferably, the material has three-dimensional polymeric networks. Particularly preferably, the material is present in the form of a sponge-like structure. In addition to such sponges, gels or
20 gelatinous materials, for example, are also usable.

25

Sponge-like structures are taken to mean according to the invention foams which consist of gas-filled spherical/polyhedral cells which are limited by highly viscous or solid cell walls. It is possible to employ
according to the invention both naturally occurring sponges and synthetically prepared sponge-like structures.

30

The sponge-like or spongy structures are prepared by methods known per se from the prior art. Depending on the starting material employed, in the simplest case a foam can be obtained by blowing, beating, shaking, spraying or stirring in the relevant gas atmosphere. In
35 the case of polymers the foam structure is produced by chemical reactions. Thus polyurethanes are foamed by adding blowing agents which decompose at a defined temperature during processing with gas formation, or by adding liquid solvents during the polymerization.

- 3 -

Foaming takes place either on leaving the extrusion dye, that is to say following the extrusion or injection molding, or in open molds. Curing takes place under the conditions characteristic of the particular
5 chemical compound of the material.

An essential prerequisite for the employability of the material is that it is compressible without breaking the cell walls. It is further essential for the
10 selection of material and manner of foam formation that it remains swellable without the cell walls being destroyed.

Preferably, the material is designed in such a manner
15 that it can be compressed to $1/2$ to $1/100$, preferably $1/4$ to $1/50$, particularly preferably $1/10$ to $1/20$, of its volume or its size. Under physiological conditions, the compressed material, after passage through the esophagus and the stomach, is to be able to expand
20 preferably to two to hundred times, particularly preferably to four to fifty times, very particularly preferably to ten to twenty times, its volume in the intestine.

25 In order to prevent constipation of the intestine or, in the worst case, even an intestinal obstruction, the volume of the decompressed materials must be chosen appropriately. In order to achieve the desired stimulating effect on the intestinal activity even with
30 relatively small embodiments of the inventive composition, a plurality of inventive compositions can be taken orally.

The material used according to the invention can have
35 any desired shape in the decompressed state. However, preference is given to cuboid or rectangular or round embodiments.

- 4 -

The material for the embodiment preferred according to the invention to be used as sponge-like structure can be natural, semisynthetic or synthetic polymers.

5 Examples of suitable synthetic polymers are polyurethanes, polyacrylates, poly(meth)acrylic esters, homopolymers and copolymers of vinyl acetate. The natural and semisynthetic polymers include, inter alia, cellulose, cellulose ethers, diethylcellulose or
10 cellulose esters, such as cellulose diacetate, cellulose triacetate, cellulose acetate propionate, cellulose acetate and cellulose butyrate. Those which are suitable according to the invention are, for example, cellulose derivatives, in particular
15 corresponding ethers, for example methyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, or sodium carboxymethyl cellulose (preferably those compounds of high viscosity); natural (anionic) mucilages, for example xanthan gum, guar gum,
20 tragacanth or alginic acid and salts thereof, and the like. In addition, the use of insoluble polysaccharides such as chitin or chitin derivatives or microcrystalline cellulose is also conceivable. Particular preference is given according to the
25 invention to unbranched high-molecular-weight polymers. In particular, those polymers can be employed according to the invention which have a fibrous structure. Examples of such materials are the scleroproteins such as keratins, conchagens, fibroin, elastins and
30 collagen.

Also, polymers which are crosslinked in a stable manner come into consideration. In particular, uronic-acid-containing polysaccharides or their salts are conceivable here that are crosslinked to one another by
35 ionic bonds and are crosslinked in a stable manner by additional covalent bonds, for example by ester bonds catalyzed by mineral acids.

- 5 -

In a particular embodiment of the invention the polymers can decompress not only in the intestine, but as early as in the stomach, and then in this state pass into the intestine and pass through this. The materials
5 which come into consideration here, in particular, are those which are scarcely observably, to not at all, degradable or absorbable in gastrointestinal fluids.

The material present in the inventive composition alone
10 can thus already exert an action in the intestine which is comparable with that of a dietary fiber and owing to which it stimulates the intestinal activity and/or contributes to the improvement and maintenance of intestinal activity. In addition, the material,
15 according to the invention, is loaded with active compounds or laxatives, more precisely in such a manner that the active compounds or laxatives are released predominantly or exclusively in the intestine.

20 In a preferred embodiment of the present invention, the material is provided with a compound which dissolves exclusively in the intestine. This is necessary in particular if the material used is degradable as early as in the stomach or small intestine.

25 The dissolution of the compound is affected by various parameters, in part also prevailing simultaneously in the intestine, for example pH, pressure, redox potential and enzymatic dissolution via the intestinal
30 flora. In addition, the residence time of the composition in the intestine also affects the rate at which the compound dissolves.

For preference, the compound dissolves at a pH between
35 5 and 10, preferably between 7 and 9, particularly preferably between 5.5 and 8.5. Dissolution in the pH environment of the intestine at a pH between 6.4 ± 0.6 and 7.0 ± 0.7 is extremely preferred.

- 6 -

The compound is applied to the material according to the invention preferably in the form of a coating which, if appropriate, can also be made up of a plurality of layers. The minimum layer thickness here
5 can vary considerably and is dependent on the film-former used and its composition. Osterwald H. et al. (Acta Pharm Technol, 1980, 26: 201-209) describes, for example, a minimum layer thickness of 46 μm for the preparation of a film-former in organic solvents,
10 preparation with an ammonium salt solution requires a layer thickness of 161 μm , as an emulsion 46 μm and as a latex dispersion 52 μm . According to the invention, the layer thickness is from 10 μm to several millimeters, preferably from 15 μm to 3 mm.

15 However, instead of a coating applied directly to the material, the material can be introduced into a container which dissolves under the above-described conditions. That is to say the container is stable in
20 the stomach, but dissolves in the intestine.

In another variant of the invention, the compound can be introduced into the material. This may be achieved, for example, by mixing the material with the compound
25 as early as when the inventive composition is prepared. Preferably, this may also be achieved by impregnating the material in a solution of the compound. Obviously, such a, for example impregnated composition can also be provided with a coating of the compound. Likewise, the
30 impregnated material can also be introduced into the above-described container. In addition, the material can be introduced into a container which itself is coated or impregnated with the compound or into which the compound is introduced.

35 The time and location of the dissolution of the compound may be influenced by the selection and combination of the compounds, which achieves targeted release of the material in the intestine and, in

- 7 -

particular, in the various intestinal sections, such as the jejunum, ileum and colon. The solubility of the compounds can depend on one or more factors, for example pH, time of exposure, redox potential of the intestine, enzymatic activities of the intestinal flora, or pressure which is produced by intestinal peristalsis. The various possibilities for controlling the release of active compounds are described extensively. The pH-dependent solubility is described, for example, in *Marvola et al.*, *Eur J Pharm Sci*, 1999, 7:259-267 and *Khan ZI et al.*, *J Controlled Release*, 1999, 58:215-222. *Pozzi F. et al.*, *J Controlled Release*, 1994, 31:99-108; *Wilding IR et al.*, *Pharmacol Ther*, 1994, 62:97-124; *Niwa K. et al.*, *J Drug Target*, 1995, 3:83-89 and US-4871549 disclose systems which release the active compounds as a function of time. Examples of systems having a combined pH and time dependency are described in *Rodriguez M. et al.*, *J Controlled Release*, 1998, 55:67-77 and *Gazzinga A. et al.*, *STP Pharm Sci*, 1995, 5:83-88. The dissolution of compounds due to a changed redox potential in the intestine is dealt with by *Bronsted H. et al.*, *Pharm Res* 1992, 9:1540-1545; *Yeh PY et al.*, *J Controlled Release*, 1995, 36:109-124; *Shanta KL et al.*, *Biomaterials*, 1995, 16:1313-1318 and *Kimura Y et al.*, *Polymer*, 1992, 33:5294-5299. Examples of systems which are released by the enzymes of the intestinal flora are described in *Ashford M et al.*, *J Controlled Release*, 1994, 30:225-232; *Fernandez-Hervas MJ et al.*, *Int J Pharm*, 1998, 169:115-119; EP-0460921; US-4432966 and *Milojevic S et al.*, *J Controlled Release*, 1996, 38:75-84. The dissolution of systems due to the pressure of intestinal peristalsis is covered in *Muraoka M et al.*, *J Controlled Release*, 1998, 52:119-129.

35

Preference is given according to the invention to the following compounds and their combinations which are, however, in no way limiting for the present invention:

- 8 -

hydroxypropyl methyl cellulose phthalate (HPMCP 55), hydroxypropyl methyl cellulose acetate succinate (Aqoat AS-MF, Aqoat AS-HF), 1:1 copolymer of methacrylic acid and ethyl acrylate (Eudragit®L), copolymer of vinyl acetate and crotonic acid (Coating CE 5142), cellulose acetate phthalate (CAP, Aquateric), methacrylate copolymers (Eudragit®S), shellac, Time Clock System®, carnauba wax, hydroxypropyl methyl cellulose (TC-5), Pulsincap®, polyethylene glycol, crosslinked polyethylene glycol, ethyl cellulose, ethyl cellulose/ethanol mixture, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, glycerol monostearate, Eudragit®E. In addition, hydrogels from azo compounds are possible, for example N-substituted methacrylamide, N-tert-butylacrylamide, acrylic acid in the presence of 4,4'-bis(methacryloylamino)azobenzenes, 4,4'-bis(N-methacryloyl-6-aminohexanoylamino)azobenzene or 3,3',5,5'-tetrabromo-4,4,4',4'-tetra(methacryloylamino)azobenzene. Examples of other compounds are unbranched polymer precursors, for example containing N,N-dimethylacrylamide, N-tert-butylacrylamide, acrylic acid, N-methacryloylglycylglycine p-nitrophenyl ester, crosslinked by suitable crosslinkers, for example N,N'-(ω-aminocaproyl)-4,4'-diaminoazobenzene and polymers containing azo compounds, for example 2-hydroxyethyl methacrylate, 4-(methacryloyloxy)azobenzene, N-(2-hydroxypropyl)methacrylamide copolymers, copolymers containing styrene and 2-hydroxyethyl methacrylate crosslinked by, for example, 4,4'-divinylazobenzene or N,N'-bis(β-sterylsulfonyl)-4,4'-diaminoazobenzene. Also, poly(ether-ester)azo polymers can also be used according to the invention, for example copolymers containing 4-[4-[(6-hydroxyhexyl)-oxy]phenyl]azobenzoic acid and 16-hydroxyhexadecanoic acid, copolymers containing 4-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]benzoic acid, 4-[4-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]phenyl]azobenzoic acid and 16-hydroxyhexadecanoic acid or 12-hydroxydodecanoic acid and segmented polyurethanes containing m-xylene

- 9 -

diisocyanate, 3,3'-dihydroxyazobenzene, polyethylene glycol or 1,2-propanediol. In addition, usable compounds are azo-compound-containing polyamides or copolymers of 4-[4-(chlorocarbonyl)phenyl]azobenzoyl chloride and α,ω -bis(aminopropyl) poly(tetramethylene oxide) and copolymers of 4-[4-chlorocarbonyl)-phenyl]azobenzoyl chloride and Jeffamine ED-600.

In addition, pectins are used, which can be additionally coated or embedded in a matrix, for example, methoxy pectin, amidated pectin, calcium pectate, pectin in combination with ethylcellulose (Aquacoat, Surelease), acrylic ester polymers (Eudragit RS30D, Eudragit NE30D). In addition, combinations of pectins with other dietary fibers are used. Examples of dietary fibers are guar (galactomannan) or chitosan, the dietary fibers themselves in turn being able to be coated or a constituent of a matrix. In this case the following substances are used as film-formers: polymethacrylate solutions, copolymers containing polyurethane and di-, oligo- or polysaccharides (galactomannans) and ethyl-galactomannans or acetylgalactomannans. In addition, cyanoacrylate, inulin, inulin suspensions containing Eudragit-RS, methacrylated inulin, chondroitin sulfate, chondroitin polymers containing 1,12-diaminododecane and dicyclohexylcarbodiimide, amorphous amylose or amorphous amylose together with other film-forming polymers are used as film-former. In addition, dextrans can be used which can be crosslinked in various ways, for example with diisocyanates, fatty acid esters, for example lauryl acid, glutaraldehyde. Conjugates of biphenylacetic acid and β -cyclodextrin, copolymers of β -cyclodextrins with methacrylic acid copolymers or acrylic acid polymers with disaccharide side groups are also used according to the invention.

The choice of compounds and their many possible combinations make possible targeted release of the material in the intestine with regards to time and

- 10 -

location. The compound can here also already comprise active compounds and/or laxatives.

The material present in the inventive composition can
5 be loaded with active compounds or laxatives in this case in a manner comparable to that which has already been described in the loading of the material with a compound. The active compounds or laxatives or combinations thereof can be introduced/applied
10 into/onto the material. This can preferably take place in the form of a coating, in which case the coating, if appropriate, can also be made up of a plurality of layers. In another variant of the invention, the active compounds and/or laxatives can be introduced into the
15 material. This may be achieved, for example, by direct mixing of the material with the active compounds and/or laxatives during the preparation of the inventive composition. Preferably, this can also be achieved by impregnating the material in a solution of the active
20 compounds and/or laxatives. Obviously, such a material, for example impregnated material, can additionally also be provided with a coating of the active compounds and/or laxatives. In addition, the material can be encased by the active compounds and/or laxatives in the
25 form of a container. In addition, the material can be introduced into a container, for example made of the abovementioned compounds which is itself coated or impregnated with the active compounds and/or laxatives or into which the active compounds and/or laxatives are
30 introduced.

In one embodiment of the present invention, the material which is thus loaded with the active compounds and/or laxatives can be compressed and in addition be
35 provided with a compound of the above-described type and in the previously described manner. The dissolution of the compound in the intestine leads to the decompression in the intestine of the material

- 11 -

obtained, together with release of the active compounds and/or laxatives.

In another embodiment of the invention, the active
5 compounds and/or laxatives can themselves be provided
with the compounds of the above-described type and in
the manner described above. The material can then be
loaded with the resulting active compounds and/or
laxatives in the manner described. The material which
10 is loaded with the active compounds and/or laxatives is
then compressed and if appropriate additionally
provided with a compound which does not dissolve until
in the intestine. The dissolution of the compound
causes the release of the active compounds and/or the
15 laxatives.

For the purposes of the invention, active compounds are
all substances having a pharmaceutical or biological
action. Examples are betamethasone, thioctic acid,
20 sotalol, salbutamol, norfenefrine, solymar, dihydro-
ergotamine, buflumedil, etofibrate, indometacin,
oxazepam, beta-acetyldigoxin, piroxicam, haloperidol,
ISMN, amitirptyline, diclofenac, nifedipine, verapamil,
pyritinol, nitrendipine, doxycycline, bromhexine,
25 methylprednisolone, clonidine, fenofibrate, allo-
purinol, pirenzepine, levothyroxine, tamoxifen, metil-
digoxin, o-(beta-hydroxyethyl)rutoside, propicillin,
aciclovir mononitrate, paracetamol, naftidrofuryl,
pentoxyfylline, propafenone, acebutolol, L-thyroxine,
30 tramadol, bromocriptine, loperamide, ketotifen,
fenoterol, Ca dobelisate, propranolol, minocycline,
nicergoline, ambroxol, metoprolol, beta-sitosterol,
enalapril hydrogen maleate, bezafibrate, ISDN,
gallopamil, xanthinol nicotinate, digitoxin, fluni-
35 trazepam, bencyclane, dexapanthenol, pindolol, lor-
azepam, diltiazem, piracetam, phenoxymethylpenicillin,
furosemide, bromazepam, flunarizine, erythromycin,
metoclopramide, acemetacin, ranitidine, biperiden,
metamizole, doxepin, dipotassium chlorazepate,

- 12 -

tetrazepam, estramustine phosphate, terbutaline, captopril, maprotiline, prazosin, atenolol, glibenclamide, cefaclor, etilefrine, cimetidine, theophylline, hydro-mirphone, ibuprofen, primidone, clobazam, oxaceprol, medroxyprogesterone, flecainide, Mg pridoxal 5-phosphate glutamate, hymecromone, etofylline clofibrate, vincamine, cinarizine, diazepam, ketoprofen, flupentixol, molsidomine, glibornuide, dimetindene, melperone, soquinolol, dihydrocodeine, clomethiazole, clemastine, glisoxepide, kallidinogenase, oxyfedrine, baclofen, carboxymethylcysteine, thiorodecine, beta-thistine, L-tryptophan, myrtol, bromalains, prenylamine, salazosulfapyridine, astemizole, sulpiride, benzerazide, dibenzepin, acetylsalicylic acid, miconazole, nystatin, ketoconazole, Na picosulfate, cholestyramine, gemfibrocil, rifampicin, fluorocortolone, mexiletine, amoxicillin, terfenadrine, mucopolysaccharide polysulfates, triazolam, mianserin, tiaprofenic acid, amezinium methyl sulfate, mefloquine, probucol, quinidine, carbamepine, Mg L-aspartate, penbutolol, piretanide, amitriptyline, cyproterone, Na valproate, mebeverine, bisacodyl, 5-aminosalicylic acid, dihydralazine, magaldrate, phenprocoumon, amantadine, naproxen, cartelol, famotidine, methyl dopa, auranofin, estriol, nadolol, levomepromazine, doxorubicin, medofenoxate, azathioprine, flutamide, norfloxacin, fendiline, prajmalium bitartrate, escin.

Further examples are the following active substances:

acetaminophen (= paracetamol), acetohexamide, acetyldigoxim, acetylsalicylic acid, acromycin, anipamil, benzocaine, beta-carotene, chloramphenicol, chlordiazepoxide, chlormadino acetate, chlorthiazide, cinnarizine, clonazepam, codeine, decamethasone, diazepam, dicumarol, digitoxin, digoxin, dihydroergotamine, drotaverine, flunitrazepam, furosemide, gramicidin, griseofluvin, hexobarbital, hydrochlorothiazide, hydrocortisone, hydroflumethazig, indimethazine, ketoprofen, lonetil, medazepam, mefruside,

- 13 -

methandrostenolone, methylprednisolone, methylsulfa-
diazine (= sulfaperin), nalidixic acid, nifedipine,
nitrazepam, nitrofurantoin, nystatin, estradiol,
papaverine, phenacetin, phenobarbital, phenylbutazone,
5 phenytoin, prednisone, reserpine, spironolactone,
streptomycin, sulfadimidine (= sulfamethazine), sulfa-
methizole, sulfamethoxazole, (= sulfameter), sulfa-
perin, sulfathiazole, sulfisoxazole, testosterone,
tolazamide, tolbutamide, trimethoprim, tyrothricin,
10 vitamins, minerals.

Active compounds which also come into consideration are
those having prophylactic action, for example in the
field of tumor therapy.

15 In addition, for the purposes of the invention active
compounds are also to be taken to mean laxatives.

The inventive composition can comprise, in addition to
20 pharmaceutically active materials and/or biologically
active materials foodstuffs or food supplements, for
example vitamins, dietary fibers, proteins, minerals
and other food constituents, taste and stimulant
substances or flavorings.

25 In addition to said substances, it is also possible to
add other ancillary substances to the material. These
may also be, for example, antioxidants, preservatives,
pigments or sweeteners. Inter alia, release-slowing
30 substances may additionally be suitable in the case
where pharmaceutically active substances are used.

In addition, the compositions according to the present
invention can additionally contain fillers, dis-
35 integrants, binders and lubricants and also excipients.

Release-slowing ancillary substances which can be used
are essentially water-insoluble ancillary substances or
mixtures thereof, such as lipids, inter alia fatty

- 14 -

alcohols, for example cetyl alcohol, stearyl alcohol and cetostearyl alcohol; glycerides, for example glycerol monostearate or mixtures of mono-, di- and triglycerides of vegetable oils; hydrogenated oils, such as hydrogenated castor oil or hydrogenated cottonseed oil; waxes, for example beeswax or carnauba wax; solid hydrocarbons, for example paraffin or earth wax; fatty acids, for example stearic acid; certain cellulose derivatives, for example ethyl cellulose or acetyl cellulose; polymers or copolymers, such as polyalkylenes, for example polyethylene, polyvinyl compounds, for example polyvinyl chloride or polyvinyl acetate, and also vinyl chloride-vinyl acetate copolymers and copolymers with crotonic acid, or polymers and copolymers of acrylates and methacrylates, for example copolymers of acrylates and methyl methacrylates.

In addition, the present invention relates to a composition for use for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements, which composition comprises a material which, if it is degradable in the stomach and/or small intestine it is provided with a compound which does not dissolve until in the intestine and which is loaded with active compounds, for example for prophylaxis, or with laxatives, in such a manner that these are predominantly or exclusively not released until in the intestine.

In addition, the present invention also relates to a process for preparing the above-described composition.

In this process, in principle, a suspension of the material is first prepared and is then freeze-dried. If appropriate, the material is comminuted in advance and/or is subjected to an alkaline and/or an acidic pretreatment. The freeze-drying is preferably carried out at -80 to +50°C, in particular -30 to +40°C.

- 15 -

In an embodiment of the inventive process in which the material is present in the form of a sponge-like structure, soluble collagen from the hides of young cattle or pigs (animals), for example, can be used. This is because the contents of soluble collagen in the hide of animals become increasingly lower with increasing age of the organism, since the collagen forms an insoluble three-dimensional network by intermolecular crosslinking. The crosslinking points are stable chemical bonds between individual collagen molecules.

Therefore, in the preparation of the required collagen suspensions for sponge preparation, the hides must originate from animals (bulls) which are one to two years old. Even here, the collagen is already forming an insoluble network. A strongly alkaline and acidic pretreatment of the hide, and mechanical forces during the preparation of the sponge suspension can cause individual chemical and physical crosslinking points in the collagen to be disrupted.

When the sponge is dried by freeze-drying and subsequent heating at 90°C to 130°C, preferably 120°C, new crosslinking points are introduced back into the sponge material by the relatively high temperatures. This causes the long-lasting insolubility of the sponge body in gastrointestinal fluids and/or water. This relative insolubility is a prerequisite for a relatively strong and stable structure which triggers a lasting stimulating effect and thus already a first laxative (purgative) action in the intestine, which is comparable with the action of dietary fibers in general. This action can be supported by the loading with active compounds and/or laxatives.

In a particularly preferred embodiment of the present invention, stably crosslinked polyuronic-acid-

- 16 -

containing polysaccharides are used, in particular alginates or their salts.

Particularly preferably, the inventive composition is
5 prepared as follows: a suspension of the material is first prepared and from this suspension, using methods known per se, a sponge- or foam-like structure is prepared. The material is then reversibly compressed. Before, during or after the preparation of the sponge-
10 like structure, the material is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine. If appropriate, a compound is applied to the material as
15 prepared and/or a compound is introduced into the material and/or this material is encased with such a compound, with this compound not dissolving until in the intestine.

20 Before, during or after the preparation of the sponge-like or foam-like structure, the material can in addition be loaded with the abovementioned compounds, pharmaceutically and/or biologically active substances, nutrients and food supplements, foodstuffs, taste and
25 stimulant substances, flavorings, ancillary substances or release-slowing substances.

All customary methods come into consideration in this regard. In the simplest case this can be carried out
30 during the sponge material preparation phase by mixing the material and the corresponding substances. Also, impregnating the material with a solution of the substances is conceivable. In addition, the abovementioned substances can be applied directly to
35 the surface of the material. This can be achieved, for example, by dipping, spraying, coating or similar methods.

The resultant material is then reversibly compressed. This can be performed by pressing, rolling or

- 17 -

comparable methods. In a particular embodiment of the invention, the material can also be compressed by chewing movements during oral intake of the material.

5 The compressed material thus prepared can, in a preferred embodiment of the invention, be encased with the above-described compound. That is to say either a container, for example a capsule casing, is produced from the compound and the material is introduced into
10 this, or the compound is directly applied to the material, for instance by dipping, spraying, coating or similar methods. In another embodiment of the invention, the compound is introduced into the material. This can be achieved by impregnation, for
15 example.

The invention is not limited to the described processes, but also applies to all other processes in which sponges, sponge-like structures or gels are
20 prepared which, due to the relative insolubility in water and/or gastrointestinal fluids, are to or can, achieve long-lasting stimulation of the intestinal activity, if appropriate mediated by appropriately suitable compounds.

25 A purpose of the inventive process is to obtain a composition that develops a long-lasting stimulating action in the intestine and at the same time is suitable for targeted release of active compounds in
30 the intestine, in particular for prophylaxis, or of laxatives. This purpose is achieved by said process steps.

The inventive composition is taken orally. The solid,
35 compressed sponge body or solid foam body passes through the mouth, throat, esophagus and stomach by addition of beverage and gentle chewing or swallowing movements and swells in the intestine, preferably back

- 18 -

to its original volume. If appropriate, the volume can also be greater than or less than the original volume.

In contrast to other food/food supplements/dietetic or medicinal products which are rapidly decomposed in the intestine or pass into the intestine already in a comminuted state, the material which is prepared in the described manner and consists of natural, semisynthetic or synthetic polymers and also stably crosslinked polymers, in particular in the form of a solid sponge body or foam body, owing to its predominantly three-dimensional polymeric network and the only slight solubility in the intestine, retains its original solid and mechanically stable structure over a period of several hours. In this case the inventive composition is present in sufficiently compressed form on passage through the esophagus and during passage through the stomach or small intestine in order to decompress in the intestine, in particular in the large intestine, and to develop the desired stimulating action.

In a particular embodiment of the invention the composition, however, can also decompress as early as in the stomach and in this state can pass into the intestine and pass through this. This applies in particular to materials which can also pass through the stomach and small intestine in decompressed form without being degraded.

For the particular case that the material, however, should already begin to degrade in the stomach or small intestine, appropriate protection from premature degradation must take place. Such a protection can be achieved by providing the material with a compound which dissolves exclusively in the intestine. In this case this compound can be incorporated/applied into/onto the material in the manner mentioned above or coated therewith.

- 19 -

Otherwise, it is, however, perfectly conceivable that the inventive composition can be provided, so to speak optionally, with an above-described compound.

- 5 A compound which may be applied/introduced onto/into the structure, or a casing of the compound offers the possibility of firstly protecting the material from premature degradation and secondly to affect the location of decompression of the material. The same
10 applies to active compounds or laxatives with which the material is loaded.

Oral intake of the inventive composition and decompression in the intestine produce an excitation of
15 the stretch receptors of the intestinal wall, which themselves initiate intestinal contractions. As a result, long-lasting excitation of intestinal activity may be achieved, resulting in a shortening of the transit time of the intestinal contents and, in
20 association with an improved water binding capacity of the stools, followed by more favorable growth conditions for the intestinal flora, as a result of which, ultimately, intestinal secretion and intestinal
25 activity can in addition be improved and maintained by the release of the active compounds or laxatives. However, in addition, active compounds can also be released in the intestine which develop their action at a site other than the intestine.

30

In addition, the present invention relates to the use of the inventive composition for preparing compositions for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements and
35 for preparing pharmaceutically active compositions and/or nutrients and/or food supplements and/or (dietetic) foods. Also, the inventive composition itself can be used for improving and maintaining intestinal activity and for improving and/or

- 20 -

normalizing bowel movements and/or for reducing the transit time of chyme in the intestine, combined with a prophylactic or laxative action. In addition, use of the inventive composition is conceivable in the fields of pharmacy and/or health and/or for nutrition and/or food supplementation. For this purpose the composition comprises the above-described active compounds or nutrients, food supplements, foods, taste and stimulant substances, flavorings or other ancillary substances.

Patent Claims:

1. A composition for improving and maintaining
intestinal activity and/or for improving and/or
5 normalizing bowel movements, characterized in that
it comprises a material which, if it is degradable
in the stomach and/or small intestine, is provided
with a compound which does not dissolve until in
the intestine, and is loaded with active
10 compounds, for example for prophylaxis, or with
laxatives in such a manner that these are
predominantly or exclusively not released until in
the intestine.
- 15 2. The composition as claimed in claim 1,
characterized in that the material has three-
dimensional polymeric networks.
3. The composition as claimed in either of claims 1
20 or 2, characterized in that the material is in the
form of a sponge-like structure.
4. The composition as claimed in one of claims 1 to
3, characterized in that the material is coated
25 with the compound.
5. The composition as claimed in one of claims 1 to
4, characterized in that the material is
introduced into a container which consists of a
30 compound which is exclusively soluble in the
intestine.
6. The composition as claimed in one of claims 1 to
5, characterized in that the compound is
35 introduced into the material.

- 22 -

7. The composition as claimed in one of claims 1 to 6, characterized in that the compound is soluble in liquid having a pH from 5 to 10.
- 5 8. The composition as claimed in one of claims 1 to 7, characterized in that the compound is soluble in liquids having a pH from 5.5 to 8.5.
- 10 9. The composition as claimed in one of claims 1 to 8, characterized in that the compound is soluble in liquids having a pH from 6.4 ± 0.6 to 7.0 ± 0.7 .
- 15 10. The composition as claimed in one of claims 1 to 9, characterized in that the material comprises natural, semisynthetic or synthetic polymers and also stably crosslinked bodies or combinations thereof.
- 20 11. The composition as claimed in one of claims 1 to 10, characterized in that the material comprises collagen, cellulose or alginate.
- 25 12. The composition as claimed in one of claims 1 to 11, characterized in that the material is compressible to one half to one hundredth, preferably one quarter to one fiftieth, particularly preferably one tenth to one twentieth of its original size.
- 30 13. The composition as claimed in one of the preceding claims 1 to 12, characterized in that the material can be decompressed in the intestine to two to one hundred times, preferably four to fifty times, particularly preferably ten to twenty times, its size in the compressed state.
- 35 14. The composition as claimed in one of the preceding claims 1 to 13, characterized in that it comprises

- 23 -

pharmaceutically and/or biologically active substances, laxatives, nutrients or food supplements, foodstuffs, taste or stimulant substances, flavorings or other ancillary substances.

5

15. The composition as claimed in one of claims 1 to 14 for use for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements, characterized in that it comprises a material which, if it is degradable in the stomach and/or small intestine, is provided with a compound which does not dissolve until in the intestine and is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine.

10

15

20

16. A process for preparing a composition for improving and maintaining intestinal activity as claimed in one of claims 1 to 15, characterized in that

25

30

35

- a) a suspension of the material is prepared,
- b) from this suspension a sponge-like or foam-like structure is prepared by methods known per se,
- c) the material is then reversibly compressed,
- d) before, during or after step b) the material is loaded with active compounds, for example for prophylaxis, or with laxatives in such a manner that these are predominantly or exclusively not released until in the intestine and
- e) if appropriate a compound is applied to this material and/or a compound is introduced into the material and/or this material is encased with such a compound, with this compound not dissolving until in the intestine.

- 24 -

17. The use of the composition as claimed in one of the preceding claims for preparing compositions for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements.
18. The use of the composition as claimed in one of the preceding claims for preparing pharmaceutically active compositions and/or nutrients and/or food supplements and/or (dietetic) foods.
19. The use of the composition as claimed in one of the preceding claims for improving and maintaining intestinal activity and for improving and/or normalizing bowel movements and/or for reducing the transit time of the chyme in the intestine, combined with a prophylactic or laxative action.
20. The use of the composition as claimed in one of the preceding claims in the fields of pharmacy and/or health and/or for nutrition and/or food supplementation.

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES
PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG(19) Weltorganisation für geistiges Eigentum
Internationales Büro(43) Internationales Veröffentlichungsdatum
15. März 2001 (15.03.2001)

PCT

(10) Internationale Veröffentlichungsnummer
WO 01/17509 A1(51) Internationale Patentklassifikation⁷: A61K 9/20,
A61P 1/00

(21) Internationales Aktenzeichen: PCT/EP00/08645

(22) Internationales Anmeldedatum:
5. September 2000 (05.09.2000)

(25) Einreichungssprache: Deutsch

(26) Veröffentlichungssprache: Deutsch

(30) Angaben zur Priorität:
199 42 424.1 6. September 1999 (06.09.1999) DE
299 15 668.0 6. September 1999 (06.09.1999) DE

(71) Anmelder und

(72) Erfinder: BEISEL, Günther [DE/DE]; Schloss Laach,
40789 Monheim (DE).

(74) Anwalt: FITZNER, Uwe; Lintorfer Str. 10, 40878 Ratingen (DE).

(81) Bestimmungsstaaten (national): AE, AG, AL, AM, AT,
AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU,CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.(84) Bestimmungsstaaten (regional): ARIPO-Patent (GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), eura-
sisches Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI,
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI-Patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE,
SN, TD, TG).

Veröffentlicht:

- Mit internationalem Recherchenbericht.
- Vor Ablauf der für Änderungen der Ansprüche geltenden Frist; Veröffentlichung wird wiederholt, falls Änderungen eintreffen.

Zur Erklärung der Zweibuchstaben-Codes, und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

(54) Title: METHOD FOR IMPROVING AND MAINTAINING BOWEL FUNCTION AS WELL AS A METHOD FOR THE PRODUCTION THEREOF(54) Bezeichnung: MITTEL ZUR VERBESSERUNG UND ERHALTUNG DER DARMTÄTIGKEIT SOWIE VERFAHREN ZU
DESSEN HERSTELLUNG

(57) Abstract: The invention relates to an agent for improving and maintaining bowel function and/or for improving and/or normalizing defecation. Said agent contains a material which decomposes in the stomach and/or the short intestinal tract and is provided with a compound which dissolves first in the intestine and contains prophylactic or laxative active ingredients which are first predominantly or exclusively released in the intestine. The invention also relates to a method for the production of the agent and its utilization.

(57) Zusammenfassung: Die vorliegende Erfindung betrifft ein Mittel zur Verbesserung und Erhaltung der Darmtätigkeit und/oder zur Verbesserung und/oder Normalisierung des Stuhlgangs, das ein Material enthält, das, sofern es im Magen und/oder Dünndarm abbaubar ist, mit einer Verbindung versehen ist, die sich erst im Darm auflöst, und mit Wirkstoffen, beispielsweise zur Prophylaxe oder mit Laxanzien derart beaufschlagt ist, daß diese überwiegend oder ausschließlich erst im Darm freigesetzt werden. Ferner betrifft die vorliegende Erfindung ein Verfahren zur Herstellung des Mittels sowie dessen Verwendung.

WO 01/17509 A1

COMBINED DECLARATION FOR PARENT APPLICATION AND POWER OF ATTORNEY
(includes Reference to PCT International Applications)

Attorney's Docket No.
FI-38

As a below named inventor, I hereby declare that:
My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **METHOD FOR IMPROVING AND MAINTAINING BOWEL FUNCTION AS WELL AS A METHOD FOR THE PRODUCTION THEREOF**

the specification of which (check only one item below):

- ☐ is attached hereto.
- ☐ was filed as United States application
Serial No. _____
on _____
and was amended
on _____ (if applicable).
- ☒ was filed as PCT international application
Number **PCT/EP00/08645**
on **September 5, 2000**
and was amended under PCT Article 19
on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a). I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY (if PCT, indicate PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
GERMANY	199 42 424.1	6 September 1999	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
GERMANY	299 15 668.0	6 September 1999	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

Combined Declaration For Parent Application and Power of Attorney (Continued)
(includes Reference to PCT International Applications)

Docket No.
FI-38

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of the application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty of disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. 120:

U.S. APPLICATIONS		STATUS(CHECK ONE)		
U.S. APPLICATION NUMBER	U.S. FILING DATE	PATENTED	PENDING	ABANDONED
PCT APPLICATIONS DESIGNATING THE U.S.				
PCT APPLICATION NO.	PCT FILING DATE	U.S. SERIAL NO.		

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. *(List name and registration number)*

FRIEDRICH KUEFFNER, REG. NO. 29,482

Send Correspondence to:

FRIEDRICH KUEFFNER
342 MADISON AVENUE, SUITE 1921
NEW YORK, N.Y. 10173

Direct Telephone Calls to:

FRIEDRICH KUEFFNER
(212) 986-3114

2	FULL NAME OF INVENTOR	<u>Family Name</u> Beisel	<u>First Given Name</u> Günther	<u>Second Given Name</u>
	RESIDENCE & CITIZENSHIP	<u>City</u> Monheim	<u>State Or Foreign Country</u> Germany <i>DK</i>	<u>Citizenship</u> German
1	POST OFFICE ADDRESS	<u>Post Office Address</u> Schloss Laach	<u>City</u> D-40789 Monheim	<u>State & Zip Code</u> Germany

Combined Declaration For Parent Application and Power of Attorney (Continued)
 (includes Reference to PCT International Applications)

 Docket No.
FI-38

2	FULL NAME OF INVENTOR	<u>Family Name</u>	<u>First Given Name</u>	<u>Second Given Name</u>
0	RESIDENCE & CITIZENSHIP	<u>City</u>	<u>State Or Foreign Country</u>	<u>Citizenship</u>
2	POST OFFICE ADDRESS	<u>Post Office Address</u>	<u>City</u>	<u>State & Zip Code</u>

2	FULL NAME OF INVENTOR	<u>Family Name</u>	<u>First Given Name</u>	<u>Second Given Name</u>
0	RESIDENCE & CITIZENSHIP	<u>City</u>	<u>State Or Foreign Country</u>	<u>Citizenship</u>
3	POST OFFICE ADDRESS	<u>Post Office Address</u>	<u>City</u>	<u>State & Zip Code</u>

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

SIGNATURE OF INVENTOR 201

SIGNATURE OF INVENTOR 202

SIGNATURE OF INVENTOR 203

DATE

DATE

DATE